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EXAMINER	
SHEN, BIN	

ART UNIT	PAPER NUMBER
1657	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/581,094	RANBY, MATS	
	Examiner	Art Unit	
	BIN SHEN	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 February 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4 and 7-17* is/are pending in the application.

4a) Of the above claim(s) *16 and 17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4, 7-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

Claims 1-4, 5-17 are currently pending. Claims 16, 17 are withdrawn from further consideration because they drawn to non-elected invention. Claims 1-4, 7-15 are presented for examination on the merits.

The amendment to specification is accepted.

Withdrawal of Rejections:

In view of applicant's argument, some of the rejections under 35 USC § 112, second paragraphs are hereby withdrawn.

In view of amended claims and applicant's argument, the rejections under 35 USC § 102(b) over Owren and Beresini are hereby withdrawn.

New Rejections due to amendments:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4, 7-9, 12, 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Beresini (1993).

On page 2240, Fig. 2, Beresini teaches a method of quantification of analyte: cyclosporine (CsA) in citrated blood (abstract and page 2236, left column, lines 7-8) by mixing 36 µl pretreated citrated blood (page 2236, right column, 2ndfull paragraph, lines 6-9) with 230 µl of reagents A and B at 37^{o}C (page 2236, right column, 2nd full paragraph, line 6), and measuring

CsA concentration (page 2237, Table 4), measuring hematocrit value from normal donors (page 2238, left column, 1st full paragraph, lines 1-2) to study the effect of hematocrit on CsA concentration (page 2238, right column, lines 2-6); the anticoagulant used is sodium citrate (page 2236, left column, line 10), the CsA concentration is calibrated with known CsA concentration in the corresponding citrated plasma (page 2237, Table 4); and the CsA (analyte) concentration is shown on page 2240, Fig. 2. **Therefore**, Beresini teaches the method of determining analyte (CsA) concentration from citrated blood sample (read as an anticoagulated plasma) by **a)** mixing 36 µl pretreated citrated blood with 230 µl of reagents A and B, and **b)** measuring CsA concentration, measuring hematocrit value of normal donors to study the effect of hematocrit on CsA concentration (part of **Claim 1**); the volume of pretreated blood sample is 36 µl which is 100% of the volume of blood, the volume of reagents A and B together is 230 µl which is 100% of the volume of reagent, the result of the analyte concentration is shown on page 2240, Fig. 2 (**Claim 2**); therefore the volume of blood is 36 µl, the volume of reagent is 230 µl , **(Claim 3),** since the pretreated citrated blood was previously diluted twice (page 2236, right column, 1st full paragraph, lines 13-14) thus it also meet the limitation of **Claim 4** where the blood volume is 18 ul (36ul diluted twice), and reagent volume of 230 ul is in the range of 150 to 600 ul; wherein the anticoagulant used is sodium citrate (**Claim 7);** the anticoagulated plasma is a fluid derived from citrated plasma (**Claim 8);** the CsA concentration is calibrated with known CsA concentration in the corresponding citrated plasma (**Claim 9**); and the measurements are performed at 37°C (**Claim 12);** the correlations between CsA (analyte) concentration and the measurement (EMIT assay) is shown on page 2240, Fig. 2 (**Claim 15).**

Beresini does not teach hematocrit measurement from the same blood sample mixture, however Beresini teaches measuring hematocrit value of normal donors to test its effect on CsA quantification (page 2238, left column, lines 1-6).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Beresini to measure hematocrit from the same blood sample mixture (**Claim 1**) because Beresini teaches measuring hematocrit value of normal donors to test its effect on CsA quantification. One would have been motivated to make the modification because Beresini et al. specifically described a method of measuring analyte concentration with

the measurement of hematocrit, and would reasonably have expected success in view of Beresini's teaching the effect of hematocrit value on CsA concentration.

Maintenance of Rejections:

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, 3, 14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 14 is rendered vague and indefinite by the word "INR". Please spell out at least at the first occurrence.

Claims 1 (in line 14), 2 (in lines 3, 5), 3 (in lines 2-3) recite the limitation "the test protocol". There is insufficient antecedent basis for this limitation in claim 1.

Applicant's arguments filed 2/17/2011 have not addressed the above rejections specifically.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Beresini and Zhang (2000).

Beresini teaches what is above as applied to claim 1.

Beresini does not teach hematocrit measurement of light with wavelengths in the range of 800 nm to 1100 nm (typical near-infrared range).

Zhang teaches blood hematocrit measurement using near-infrared radiation that provide acceptable accuracy (page 295, left column, line 6, page 299, right column, end of 1st full paragraph).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Beresini to measure hematocrit with wavelengths in the range of 800 nm to 1100 nm (**Claim 11**) because Zhang the possibility and accuracy of measurement of hematocrit with near-infrared wavelength. One would have been motivated to make the modification because Beresini et al. specifically described a method of measuring analyte concentration with the measurement of hematocrit, and would reasonably have expected success in view of Zhang's teaching of using 800 nm to 1100 nm wavelength to measure hematocrit.

Applicant's arguments filed 2/15/2011 have been fully considered but they are not persuasive.

Applicant argues that Beresini does not teach two measurements from the same blood sample and that the assay is not affected by hematocrit value, thus combining with the teaching of Zhang does not bring a person skilled in the arts any closer to the present invention.

It is the examiner's position that Beresini teaches measuring CsA concentration (page 2237, Table 4), measuring hematocrit value from normal donors (page 2238, left column, 1st full paragraph, lines 1-2) to study the effect of hematocrit on CsA concentration (page 2238, right column, lines 2-6). Therefore, Beresini combined the two measurements to study the effect of hematocrit on CsA concentration, thus a person of ordinary skill in art, upon reading the reference, would has good reason to make two measurement from one blood sample to improve accuracy which is within his/her technical grasp, if this leads to the anticipated success, it is likely the measurement not of innovation but of ordinary skill and common sense because two types of data is used in Beresini to study the effect of hematocrit on CsA concentration in blood. Zhang is cited for teaching of hematocrit measurement using near-infrared radiation that provide acceptable accuracy (page 295, left column, line 6, page 299, right column, end of 1st full

paragraph), and because Beresini measures hematocrit value form normal donors, thus near-infrared radiation can be used to improve accuracy of the measurement.

Claims 1, 13, 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Beresini and Potzsch (1997).

Beresini teaches what is above as applied to claims 1.

Beresini does not teach the reagent contains 0.1 g/L or more fibrinogen, the analyte concentration is expressed in INR.

Potzsch teaches a method of monitoring hirudin concentration (page 380, Fig.4) in citrated blood sample (page 375, line 3) by measuring snake venom enzyme ecarin clotting time (page 376, Table 1) expressed in INR (page 380, Fig. 4, **Claim 14**). The minimal concentration of fibrinogen for the assay is 50 mg/dl (**0.5 g/L**, page 376, 2nd paragraph, line 10, page 377, Fig. 1, **Claim 13**).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Beresini to use above minimal concentration of fibrinogen in the reagent (above 0.1g/L, **Claim 13**) to measure the concentration of different analyte and expressed the concentration in INR (**Claim 14**) because Potzsch teaches monitoring hirudin concentration by measuring snake venom enzyme ecarin clotting time expressed in INR with above minimal concentration of fibrinogen in the sample. One would have been motivated to make the modification because Beresini et al. specifically described a method of determining CsA concentration, and would reasonably have expected success in view of Potzsch's testing of the minimal concentration of fibrinogen in the sample and to express the analyte's concentration in INR.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments filed 2/15/2011 have been fully considered but they are not persuasive.

Applicant argues that Beresini can not be combined with Potzsch because Potzsch mention nothing on analysis of blood, and there is no mention of adding fibrinogen to the reagent as in claims 13, no mention of the possibilities of re-expressing INR into PT% as in claim 14.

It is the examiner's position that Potzsch teaches a method of monitoring hirudin concentration (page 380, Fig.4) in citrated blood sample (page 375, line 3) by measuring snake venom enzyme ecarin clotting time (page 376, Table 1) expressed in INR (page 380, Fig. 4), the influence of different fibrinogen concentration on the ECT is investigated (page 376, 2nd paragraph, lines 8-9). Therefore, blood sample is used in the analysis, different fibrinogen concentrations is shown (on page 377, Fig. 1, legend, line 5). Since the clotting time is expressed in INR, therefore the PT% can be calculated from the expressed INR because it is within the technical grasp of a person of ordinary skill in the art to use different but functionally equivalent ways to express the measured results.

Conclusion

Claims 1-4, 7-15 are rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning rejections or objections in this communication or earlier communications from the examiner should be directed to Bin Shen, whose telephone number is (571) 272-9040. The examiner can normally be reached on Monday through Friday, from about 9:00 AM to about 5:30 PM. A phone message left at this number will be responded to as soon as possible (i.e., shortly after the examiner returns to her office).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached at (571) 272-0925.

B Shen
Art Unit 1657

/Karen Cochrane Carlson/

Primary Examiner, Art Unit 1656